Message

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Subject: Chloroprene PBPK: model code & output table

Jerry, all,

Typo: A minor thing is that the lowest mouse concentration in the table on p. 21 should be 12.8 ppm (what is used in the code, bioassay concentration), not 12.3 ppm.

Scaling of "KF" values: I had reviewed the chloroprene.model file back in the summer, and there's something I didn't catch then, which I think will have minor numerical impact, but is a technical issue. The pseudo-first-order rate terms for metabolism in the lung and kidney (KFLUC and KFKIC) are presumed to represent Vmax/Km in the case where the data were not sufficient to identify separate values for the two parameters. We assume it's still CYP-mediated metabolism, though a Km could not be identified. In that case they should be scaled as BW^0.75, not BW^1.

In the spreadsheet, Supp Mat D…, for example the units shown in cells AC21 (KFKIC for female mouse), U32 and U37 (KFLUC for female and male rats) indicate this was initially intended, though KFLUC for humans is just shown as (L/h/kg BW) there.

The calculations in Supp Mat D all normalize to BW^1 and the units shown in Table S-4 in Supp Mat A match that, and the calculation of the scaled values in the code multiplies by BW^1. So those pieces are self-consistent. But to the extent that animal BWs in bioassays differ from the standard values used to estimate the extrapolation factor, the scaling in the model and calculation of scaled values in the spreadsheet should be by BW^0.75, since it's a metabolic rate.

I also note that the value of KFLUC for the male rat lung in Supp Mat A, Table S-4, is "0.084" (value for female rats), but the value in the spreadsheet is 0.092.

Other typo: On p. 18 of the report, we have the following text:
Using the human value of A1 (0.00143), together with the estimated values of Vmax and Km in the human liver from the MCMC analysis (0.053 µmol/hr/mg protein and 0.38 µmol/L), results in a metabolic clearance in the lung of 0.20 L/hr/g microsomal protein. ….
The mean liver Vmax is 0.052, not 0.053.

-Paul